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[Two of the authors respond:]

The issues Dr. Ohlsson and Ms. Myhr raise strengthen the conclusions of our study.

The related meta-analyses from the Oxford perinatal database,[1-3] which we used to identify studies in progress but not meta-analyses, used different summation procedures from ours but also suggested a favourable effect of intrapartum penicillin in preventing early-onset GBS infection.

We identified the six RCTs Ohlsson and Myhr cite.[4-9] They included a study addressing the effect of intrapartum prophylaxis on puerperal infection instead of early-onset disease,[4] a letter to the editor[5] and a related thesis,[6] an abstract[7] and two interim reports.[8-9] The results of the studies addressing early-onset GBS infection[5-9] were all published on completion of the studies,[10-13] and the final publications are included in our meta-analysis.

Our analysis is not affected by whether Boyer and Gotoff[11] examined their data several times, thus increasing the chance of a type I error, without adjusting their significance level.[14] Our calculations are based on raw data and are not affected by *p* values. Whether these researchers examined the control group more closely after interim analysis is speculation.

Although our definition of invasive disease was not published, we defined it as a positive culture result from blood or cerebrospinal fluid (CSF) samples, soluble antigen in CSF or urine in the presence of clinical evidence of GBS infection, or a positive culture result from postmortem samples taken from previously sterile sites. In the study by Boyer and Gotoff[11] the neonate with bacteremia but no obvious symptoms of sepsis would be regarded as having invasive GBS infection, particularly because the infant was one of five born to mothers at high risk of transmitting GBS infection, given that labour was premature (which may be a symptom of GBS infection) and that there was prolonged rupture of membranes. The natural course of untreated asymptomatic bacteremia is likely to be metastatic infection (especially meningitis), fulminant disease and death.[15]

With respect to the two studies that used latex agglutination tests, Morales, Lim and Walsh[12] stated that "neonatal sepsis was diagnosed on the basis of positive results of body fluid cultures." Although Tuppurainen and Hallman[10] used the latex agglutination test, they did not indicate that a positive result was part of their diagnostic criteria for early-onset GBS infection. Their criteria were severe symptoms (including respiratory distress and signs of shock within 48 hours after birth), a positive culture result from blood samples or presence of group B streptococci in superficial cultures, and leukopenia or elevated C-reactive protein level.

We calculated ORs using the number of infants as well as the number of mothers as denominators; because these denominators differed only slightly, the results were almost identical (common OR 0.03, 95% confidence interval [CI] 0.0013 to 0.17). However, we felt that the number of infants was a less reliable denominator because data on multiple pregnancy were available from only three of the seven studies in our meta-analysis.[11-13] In the remaining studies[10,12,16,17] the number of births and mothers appeared to be the same, but this would need to be verified.

Ohlsson and Myhr appear to have misinterpreted the outcome measure in the study by Boyer and Gotoff.[11] The authors examined the effect of intrapartum chemoprophylaxis on bacteremia by taking blood samples for culture at birth; thus, postnatal administration of antibiotics would not affect this outcome measure. Even if this study were removed from the meta-analysis the pooled OR of the remaining RCTs would still show a beneficial effect of penicillin (OR 0.06, 95% CI 0.003 to 0.49).

Ohlsson and Myhr concur with us that there is no gold standard for assessing the quality of an RCT. We are pleased that our method was explicit enough that they could easily follow it and compare it with another, which yielded a similar ranking. With respect to the nonblinded, nonrandomized example given by them, we agree that a rating of 0.25 (out of a maximum of 1) does not suggest a high-quality study.

We agree that the assignment of patients allergic to ampicillin to the control group in one study violated randomization.[12] The importance of such a systematic bias depends on its effect on the results. There is no known biologic reason to expect women allergic to ampicillin to be at greater risk of delivering infants with GBS infection and, therefore, no reason to believe that the study would have had more cases of GBS infection in the control group.

It is well recognized that a lack of blinding introduces a risk of diagnostic suspicion bias;[18] however, a careful examination of each study shows the potential effect of this bias on the results. For example, in the study by Boyer and Gotoff[11] if single standard blood samples were taken from all infants at birth to culture for bacteremia, this bias would be less relevant. Thus, although blinding is important, its effect in re-

ducing diagnostic suspicion bias is usually viewed in the context of the outcome measures. This highlights the problems associated with considering bias in general terms rather than assessing its effect on the specific questions addressed.

We agree that Boyer and Gotoff[11] did not analyse patients on an intent-to-treat basis; the pros and cons of this approach are well documented.[19]

The main issues Ohlsson and Myhr raise paradoxically strengthen our conclusions. The independently conducted meta-analyses[1-3] they found also showed a beneficial effect of intrapartum penicillin prophylaxis. Their search identified no additional RCTs and thus confirms the adequacy of our search. They concur with the ranking of quality of the main studies. Their comments on problems and biases in the primary studies have enabled us to clarify our methods and show that our conclusions remain robust.

Their accusation that the studies included in our meta-analysis are of poor quality is unfortunate, given the evidence and the acknowledgement that there is no gold standard for assessing quality. We believe that our meta-analysis is scientifically sound and that it will facilitate decision making in Canada. As well, the studies included formed the basis for current consensus statements on intrapartum prophylaxis of early-onset GBS infection.[20-22]

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Medic Alert bracelets

On behalf of the Canadian Medic Alert Foundation I applaud the article "Fatal anaphylactic reactions to food in children" (*Can Med Assoc J* 1994; 150: 337–339), by the Allergy Section of the Canadian Paediatric Society, particularly the statement that "all patients at risk of a lethal allergic reaction to food should wear a Medic Alert bracelet." Other patients who should wear these bracelets include those with implants, transplanted organs, pacemakers, epilepsy and diabetes, those receiving multiple drug therapy and those with dementia, who may be inclined to wander.

Although the authors kindly provide the address for the foundation, the toll-free telephone number may be even more helpful to physicians and patients who want to apply for membership: (800) 668-1507.

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